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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,672	04/18/2006	Rino Rappuoli	002441.00121	7180

27476 7590 03/03/2009

NOVARTIS VACCINES AND DIAGNOSTICS INC.
INTELLECTUAL PROPERTY R338
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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

MAIL DATE	DELIVERY MODE
03/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,672	RAPPUOLI ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *5,6,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-15 and 18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *031105 & 041708*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 03/11/05, 10/23/08 and 12/09/08.

Election

2) Acknowledgment is made of Applicants' election filed 10/23/08, with traverse, in response to the lack of unity mailed 06/24/08. Applicants have elected invention I, claims 1-15. Because Applicants did not distinctly and specifically point out the supposed errors in the lack of unity, the election has been treated as an election without traverse (M.P.E.P § 818.03(a)).

Applicants have further elected, with traverse, the serotype Ia GBS saccharide antigen species, the GBS80 plus GBS322 polypeptide antigen combination species; and the diphtheria toxoid and CRM197 carrier protein species. Applicants' traversal is on the following grounds: MPEP 803.02 states that if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the Office must examine all the members of the Markush group in the claim on the merits. Applicants state that claim 18 recites only 18 GBS polypeptide species and claim 1 recites only three GBS saccharide antigen species, and therefore would not present a serious examination burden. Applicants argue that the species are closely related in that they all originate from Group B streptococcus and that a search for immunogenic compositions comprising GBS80 would necessarily search for immunogenic compositions comprising GBS80 *and* any other recited GBS polypeptide antigens.

Applicants' arguments have been carefully considered, but are not persuasive. The number of species in the instant application is neither sufficiently few in number nor so closely related that a search *and* examination of the entire claims can be made without serious search burden and without serious examination burden. As set forth previously, the various saccharide antigen species and the GBS polypeptide antigen species do not share a significant common structural element, requiring separate individual structure searches. The species have mutually exclusive structural and/or antigenic or immunogenic characteristics. A search for Group B streptococcus alone, or a search for GBS80 alone would not necessarily find all relevant prior art

on each of the saccharide antigen species and each of the non-GBS80 polypeptide antigen species. For these reasons, the species election requirement set forth in the instant application for saccharide antigen species and polypeptide antigen species is proper and is hereby made FINAL. However, Applicants should note that the examination of the carrier protein species has been further extended to tetanus toxoid.

Status of Claims

3) Claims 1, 3-6, 8, 9 and 17 have been amended via the amendment filed 12/19/08.

New claims 18-23 have been added via the amendment filed 12/19/08.

Claims 1-23 are pending.

Claims 5, 6, 16 and 17 are withdrawn from consideration as being directed to a non-elected invention and/or species. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1-4, 7-15 and 18-23 are under examination. A First Action on the Merits on these claims is issued.

Sequence Listing

4) Acknowledgment is made of Applicants' submission of the sequence listing and CRF which have been entered on 03/24/05.

Information Disclosure Statements

5) Acknowledgment is made of Applicants' Information Disclosure Statements filed 03/11/05 and 04/17/09. Except for a duplication citation, the information referred to therein has been considered and a signed copy is attached to this Office Action.

Priority

6) The instant application is the national stage 371 application of the international application, PCT/US2003/029167, filed 09/15/03 and claims priority to the provisional application 60/410,839 filed 09/13/02.

Objection(s) to Specification

7) The specification is objected to for the following reason(s):

(a) The use of the trademarks has been noted in this application. For example, page 22, lines 6 and 10: 'Tween 80' and 'Span 85'. The trademark recitation should be capitalized.

Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification and make necessary changes wherever trademark recitations appear.

(b) The incorporation of essential material in the specification by reference to unpublished U.S. applications, foreign applications or patents, or to a publication is improper. See for example, pages 27, 29 and 30; and lines 9, 10 and 20 of page 4 of the specification. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the Applicant, or a practitioner representing the Applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

Rejection(s) under 35 U.S.C. § 101

8) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

9) Claim 1 and the claims dependent therefrom are rejected under 35 U.S.C § 101 as being directed to a non-statutory subject matter.

Claim 1 does not sufficiently distinguish the claimed composition over naturally occurring GBS bacterium, as it exists naturally, because the claim does not particularly point out any non-naturally occurring differences between the claimed product(s) and the naturally occurring GBS bacterium that comprises therein a non-isolated saccharide antigen and non-isolated GBS 80 and GBS 322 polypeptides or fragments thereof. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980)*. The claims should be amended to indicate the hand of the inventor, e.g., by insertion of --an isolated GBS saccharide antigen-- and --at least two isolated GBS polypeptide antigens-- in lines 1 and 2 of the claim. Applicants should make

sure that descriptive support exists for such a limitation in the instant application, as originally filed. See MPEP 2105.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

10) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

11) Claims 1-4, 7-15 and 18-23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 1-4, 7-10, 18 and 19 are vague and indefinite in the abbreviated limitation: 'GBS', because it is unclear what does this limitation encompass. It is suggested that the abbreviation be recited as a full terminology at first occurrence in the base claim, with its abbreviated recitation retained therein in parentheses.

(b) Claim 2 is indefinite and/or incorrect in the limitation: 'GBS polypeptide of .... serogroup II', because it is unclear what does the limitation 'serogroup II' encompass. Is this some kind of serogroup II bacterium? It is further unclear how the limitation 'serogroup' differs from the limitation in the base claim, 'serotype'.

(c) Claim 1 is incorrect in the limitation: 'two polypeptide' (see line 4), because two represents a pleural limitation. It is suggested that Applicants replace the above-identified limitation with the limitation --two polypeptides--.

(d) Claim 1 is vague and confusing in the Markush limitation: 'selected from the antigen group consisting of'. For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the above-identified limitation with the limitation --selected from the group consisting of--.

(e) Claims 1, 3, 4, 8, 9 and 18 are vague and indefinite in the limitation 'as represented by' because it is unclear whether it represents open or closed claim language. For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the above-identified limitation with the limitation --set forth as--.

(f) Claims 1 and 4 are vague and indefinite in the limitation: 'fragments thereof' because it is unclear what is encompassed in this limitation. What constitutes 'fragments', and how much of the polypeptide's original structure has to be retained such that the resulting polypeptides can be considered 'fragments' is not clear. The metes and bounds of the structure encompassed in the limitation 'fragments' are indeterminate. Does a single amino acid constitute a 'fragment'?

(g) Analogous rejection and criticism apply to claims 2 and 3 with regard to the limitation: 'fragment thereof'.

(h) Claim 1 is indefinite, inconsistent, and confusing in scope in the limitations: 'saccharide antigen' and 'saccharide' as well as 'polypeptide antigens' and 'polypeptide'. It is unclear how a 'saccharide antigen' differs in scope from a 'saccharide' and how 'polypeptide antigens' differ from 'polypeptides' in terms of scope.

(i) Analogous rejection and criticism apply to claim 19 with regard to the limitations: 'GBS saccharide antigen' and 'saccharide'.

(j) Claims 1, 2 and 3 are indefinite because the claims lack proper antecedent basis in the limitation: 'said GBS polypeptide antigens'. For proper antecedence, it is suggested that Applicants replace the above-identified limitation with the limitation --said at least two GBS polypeptide antigens--.

(k) Claim 4 is improperly broadening in scope in the limitation: said GBS polypeptide antigens comprise a combination of 'two GBS antigens or fragments thereof' (see line 2). The latter limitation 'GBS antigens' is broader than the earlier limitation 'GBS polypeptide antigens'.

(l) Claim 10, which depends from claim 1, is indefinite because it lacks proper antecedent basis in the limitation: 'at least one GBS polypeptide antigen'. For proper antecedence, it is suggested that Applicants replace the above-identified limitation with the limitation --at least one of the GBS polypeptide antigens--.

(m) Claim 12 is incorrect in the limitations: '*N. meningitides*' and 'pertusis'. The two terms are misspelled.

(n) Claim 18 is indefinite, confusing and appears to have improper antecedent basis in the limitation: 'the two GBS polypeptide antigens'. Claim 18 depends from claim 1 which

includes the limitations: 'at least two polypeptide antigens' and 'at least two polypeptide', but not 'two polypeptide antigens'.

(o) Claims 2-4, 7-15 and 18-23, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

12) The following is a quotation of the appropriate paragraph(s) of 35 U.S.C. § 102 that form the basis for the rejection(s) under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13) Claims 1-4 and 10-13 are rejected under 35 U.S.C § 102(b) as being anticipated by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994).

It is noted that the limitation 'fragment thereof' lacks a structure limit, size limit, or length limit, and therefore encompasses a single amino acid, or a dipeptide. It is further noted that the polypeptide antigens or fragments thereof are not required to be isolated and/or purified.

Paoletti *et al.* taught an immunogenic and protective multivalent vaccine comprising type Ia GBS capsular polysaccharide conjugated to tetanus toxoid carrier protein. The tetravalent vaccine comprised individually prepared type II GBS-TT, type Ib GBS-TT and type III GBS-TT conjugates, each containing individually conjugated tetanus toxoid. See abstract; Materials and methods; and Results. A single amino acid residue from the tetanus toxoid of a non-type Ia GBS conjugate, such as type II GBS-TT conjugate, serves inherently as 'a fragment' of a GBS polypeptide of serogroup II as recited in claim 2. Likewise, a single amino acid from the tetanus toxoid of each of the other non-type Ia GBS conjugates, such as type III and Ib GBS-TT conjugates, serves inherently as 'a fragment' of SEQ ID NO: 2 (GBS 80 polypeptide antigen) and 'a fragment' of SEQ ID NO: 18 (GBS 322 polypeptide antigen) as recited in claim 1.

Claims 1-4 and 10-13 are anticipated by Paoletti *et al.*

Rejection(s) under 35 U.S.C § 103

14) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

15) Claims 1-4, 7, 10-15 and 18-23 are rejected under 35 U.S.C § 103(a) as being unpatentable over CHIRON S.P.A (WO 02/34771 A2 – Applicants' IDS) ('771) in view of Wessels *et al.* (*Infect. Immun.* 61: 4760-4766, 1993).

CHIRON S.P.A ('771) disclosed a composition comprising two or more GBS proteins or sequences comprising GBS 80 and GBS 322 proteins having SEQ ID NO: 8780 (i.e., the instantly recited SEQ ID NO: 2) and SEQID NO: 8540 (i.e., the instantly recited SEQ ID NO: 322), or fragments thereof. See claim 28; lines 9-10 of page 9; pages 7, 8, 2997 and 2992. The composition further comprises a saccharide antigen and diphtheria antigens. See claim 27 and page 8. When a saccharide is included in the composition, it is preferably conjugated to a carrier protein such as CRM197, diphtheria toxoid, or tetanus toxoid in order to enhance immunogenicity. See page 8. A single amino acid residue from additional GBS proteins or sequences present in the prior art composition inherently serves as a fragment of a GBS polypeptide of serogroup II. The prior art SEQ ID NO: 8780 and SEQ ID NO: 8540 show 100% sequence identity with the instantly recited SEQ ID NO: 2 and SEQ ID NO: 18 respectively as depicted below:

```
ABP29802
AC   ABP29802
DT   15-JUN-2007  (revised)
DT   02-JUL-2002  (first entry)
DE   Streptococcus polypeptide SEQ ID NO 8780
KW   Streptococcus; GAS; GBS; group B streptococcus; Streptococcus
agalactiae;
KW   group A streptococcus; Streptococcus pyogenes; antibacterial;
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KW antiinflammatory; infection; vaccine; meningitis; gene therapy; BOND_PC;
KW cell wall surface anchor family protein; hypothetical protein
KW hypothetical protein gbs0628 [Streptococcus agalactiae NEM316]; Unknown;
KW Unknown [Streptococcus agalactiae NEM316]
OS Streptococcus agalactiae
PN WO200234771-A2
PD 02-MAY-2002
PF 29-OCT-2001; 2001WO-GB004789
PR 27-OCT-2000; 2000GB-00026333
PR 24-NOV-2000; 2000GB-00028727
PR 07-MAR-2001; 2001GB-00005640
PA (CHIR) CHIRON SPA
PA (GENO-) INST GENOMIC RES
PI Telford J, Masignani V, Margarit Y RosI, Grandi G, Fraser C;
PI Tettelin H
DR WPI; 2002-352536/38
DR N-PSDB; ABN70433
DR PC:NCBI; gi22533660
PT New Streptococcus protein for the treatment or prevention of infection
or
PT disease caused by Streptococcus bacteria, such as meningitis, and for
PT detecting a compound that binds to the protein.
PS Claim 1; Page 3995; 4525pp; English.
CC The invention relates to a protein (ABP25413-ABP30895) from group B
CC streptococcus/GBS (Streptococcus agalactiae) or group A
streptococcus/GAS
CC (Streptococcus pyogenes), comprising one of 5483 sequences (S1), given
in
CC the specification. The proteins have antibacterial and antiinflammatory
CC activity. (I), nucleic acids encoding (I), ABN66044-ABN71526 and
CC antibodies that bind (I) are used in the manufacture of medicaments for
CC the treatment or prevention of infection or disease caused by
CC Streptococcus bacteria, particularly S. agalactiae and S. pyogenes.
CC Nucleic acids encoding (I) are used to detect Streptococcus in a
CC biological sample. (I) is used to determine whether a compound binds to
CC (I). A composition comprising (I) or a nucleic acid encoding (I), may be
CC used as a vaccine or diagnostic composition. The disease caused by
CC Streptococcus that is prevented or treated may be meningitis. Nucleic
CC acid encoding (I) may be used to recombinantly produce (I) and may be
CC used in gene therapy. Antibodies to (I) are used for affinity
CC chromatography, immunoassays, and distinguishing/identifying
CC Streptococcus proteins
SQ Sequence 554 AA;

Query Match 100.0%; Score 554; DB 5; Length 554;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 554; Conservative 0; Mismatches 0; Indels 0; Gaps
0.

Qy 1 MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSY 60
||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 1 MKLSKKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSY 60

Qy 61 KSEITSNGGIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAAD 120

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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          61 KSEITSNGGIENKDGEVISNYAKLGDNVKGLQGVQFKRYKVKTDISVDELKKLTTVEAAD 120

Qy         121 AKVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLEL 180
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         121 AKVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLEL 180

Qy         181 PVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLGQDDAGYTIGEEFKWFLKSTIPANL 240
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         181 PVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLGQDDAGYTIGEEFKWFLKSTIPANL 240

Qy         241 GDYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNTLKITFKPEKFK 300
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         241 GDYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNTLKITFKPEKFK 300

Qy         301 EIAELLKGMTLVKNQDALDKATANTDDAAFLEIPVASTINEKAVLGKAIENTFELQYDHT 360
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         301 EIAELLKGMTLVKNQDALDKATANTDDAAFLEIPVASTINEKAVLGKAIENTFELQYDHT 360

Qy         361 PDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKA 420
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         361 PDKADNPKPSNPPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKA 420

Qy         421 NTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVI 480
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         421 NTNKNYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVI 480

Qy         481 PDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPSIPNTGGIGTAIFVAIGAAVM 540
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         481 PDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPSIPNTGGIGTAIFVAIGAAVM 540

Qy         541 AFAVKGMKRRTKDN 554
                ||||||||||||||
Db         541 AFAVKGMKRRTKDN 554
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ABP29682
AC   ABP29682
DT   02-JUL-2002  (first entry)
DE   Streptococcus polypeptide SEQ ID NO 8540.
KW   Streptococcus; GAS; GBS; group B streptococcus; Streptococcus
agalactiae;
KW   group A streptococcus; Streptococcus pyogenes; antibacterial;
KW   antiinflammatory; infection; vaccine; meningitis; gene therapy.
OS   Streptococcus agalactiae
PN   WO200234771-A2
PD   02-MAY-2002
PF   29-OCT-2001; 2001WO-GB004789
PR   27-OCT-2000; 2000GB-00026333
PR   24-NOV-2000; 2000GB-00028727
PR   07-MAR-2001; 2001GB-00005640
PA   (CHIR ) CHIRON SPA
PA   (GENO-) INST GENOMIC RES.
PI   Telford J,  Masignani V,  Margarit Y RosI,  Grandi G,  Fraser C;
PI   Tettelin H
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DR   WPI; 2002-352536/38
DR   N-PSDB; ABN70313
PT   New Streptococcus protein for the treatment or prevention of infection or
PT   disease caused by Streptococcus bacteria, such as meningitis, and for
PT   detecting a compound that binds to the protein.
PS   Claim 1; Page 3964; 4525pp; English.
CC   The invention relates to a protein (ABP25413-ABP30895) from group B
CC   streptococcus/GBS (Streptococcus agalactiae) or group A
streptococcus/GAS
CC   (Streptococcus pyogenes), comprising one of 5483 sequences (S1), given
in
CC   the specification. The proteins have antibacterial and antiinflammatory
CC   activity. (I), nucleic acids encoding (I), ABN66044-ABN71526 and
CC   antibodies that bind (I) are used in the manufacture of medicaments for
CC   the treatment or prevention of infection or disease caused by
CC   Streptococcus bacteria, particularly S. agalactiae and S. pyogenes.
CC   Nucleic acids encoding (I) are used to detect Streptococcus in a
CC   biological sample. (I) is used to determine whether a compound binds to
CC   (I). A composition comprising (I) or a nucleic acid encoding (I), may be
CC   used as a vaccine or diagnostic composition. The disease caused by
CC   Streptococcus that is prevented or treated may be meningitis. Nucleic
CC   acid encoding (I) may be used to recombinantly produce (I) and may be
CC   used in gene therapy. Antibodies to (I) are used for affinity
CC   chromatography, immunoassays, and distinguishing/identifying
CC   Streptococcus proteins
SQ   Sequence 432 AA
  Query Match             100.0%;  Score 432;  DB 5;  Length 432;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches  432;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps 0

Qy          1 MNKKVLLTSTMAASLLSVASVQAQETDTTWTARTVSEVKADLVKQDNKSSYTVKYGDTLS 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MNKKVLLTSTMAASLLSVASVQAQETDTTWTARTVSEVKADLVKQDNKSSYTVKYGDTLS 60

Qy         61 VISEAMSIDMNVLAKINNIADINLIYPETTLTVTYDQKSHTATSMKIETPATNAAGQTTA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 VISEAMSIDMNVLAKINNIADINLIYPETTLTVTYDQKSHTATSMKIETPATNAAGQTTA 120

Qy        121 TVDLKTNQVSVADQKVSLNTISEGMTPEAATTIVSPMKTYSSAPALKSKEVLAQEQAVSQ 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 TVDLKTNQVSVADQKVSLNTISEGMTPEAATTIVSPMKTYSSAPALKSKEVLAQEQAVSQ 180

Qy        181 AAANEQVSPAPVKSITSEVPAAKEEVKPTQTSVSQSTTVSPASVAAETPAPVAKVAPVRT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AAANEQVSPAPVKSITSEVPAAKEEVKPTQTSVSQSTTVSPASVAAETPAPVAKVAPVRT 240

Qy        241 VAAPRVASVKVVTPKVETGASPEHVSAPAVPVTTTSPATDSKLQATEVKSVPVAQKAPTA 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 VAAPRVASVKVVTPKVETGASPEHVSAPAVPVTTTSPATDSKLQATEVKSVPVAQKAPTA 300

Qy        301 TPVAQPASTTNAVAAHPENAGLQPHVAAYKEKVASTYGVNEFSTYRAGDPGDHGKGLAVD 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 TPVAQPASTTNAVAAHPENAGLQPHVAAYKEKVASTYGVNEFSTYRAGDPGDHGKGLAVD 360
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Qy        361 FIVGTNQALGNKVAQYSTQNMAANNISYVIWQQKFYSNTNSIYGPANTWNAMPDRGGVTA 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 FIVGTNQALGNKVAQYSTQNMAANNISYVIWQQKFYSNTNSIYGPANTWNAMPDRGGVTA 420

Qy        421 NHYDHVHVSFNK 432
              ||||||||||||
Db        421 NHYDHVHVSFNK 432
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CHIRON S.P.A ('771) does not expressly identify the saccharide antigen conjugated to CRM197 or diphtheria toxoid to be type Ia saccharide of Group B streptococci.

However, the use type Ia GBS capsular saccharide in a conjugate vaccine was already known in the art at the time of the invention. For example, Wessels *et al*. taught a vaccine comprising type Ia GBS capsular polysaccharide conjugated to tetanus toxoid which vaccine stimulated protective opsonic antibodies against the GBS. Wessels *et al*. showed that type Ia GBS capsular polysaccharide not only elicited protective antibodies type Ia strains, but also advantageously against GBS Ib strains. See abstract; Materials and Methods; and Results.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace the generic saccharide antigen in CHIRON S.P.A's ('771) saccharide- CRM_{197} conjugate with Wessels' type Ia GBS capsular polysaccharide to produce the instant invention with a reasonable expectation of success. Given that the type Ia GBS capsular polysaccharide was already used to produce a conjugate vaccine, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of eliciting not only protective antibodies against type Ia Group B streptococci, but also advantageously against type Ib Group B streptococci.

Claims 1-4, 7, 10-15 and 18-23 are *prima facie* obvious over the prior art of record.

Claim Objection(s)

16) Claims 1, 3, 4, 8, 9 and 18 are objected to for not leaving a space after the limitation 'SEQ ID NO:'.

Remarks

17) Claims 1-4, 7-15 and 18-23 stand rejected.

18) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Central Fax number, (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

19) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

20) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

February, 2009